

# An Epidemiologic Study of the Association between Free Recall Dichotic Digits Test Performance and Vascular Health

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Mary E. Fischer\*  
Karen J. Cruickshanks\*†  
Lauren K. Dillard‡  
David M. Nondahl\*  
Barbara E. K. Klein\*  
Ronald Klein\*  
James S. Pankow§  
Ted S. Tweed\*  
Carla R. Schubert\*  
Dayna S. Dalton\*  
Adam J. Paulsen\*

## Abstract

**Background:** Associations between vascular health–related factors and hearing loss defined using audiometric pure-tone thresholds have been found. Studies have not focused on a potential relationship between vascular health–related factors and central auditory processing.

**Purpose:** The aim of this study was to evaluate, on a population level, the relationship of vascular health–related factors with central auditory function.

**Research Design:** A cross-sectional, population study.

**Study Sample:** Subjects were participants in the Epidemiology of Hearing Loss Study (EHLS) or the Beaver Dam Offspring Study (BOSS)—prospective studies of aging and sensory loss. BOSS participants were the adult offspring of participants in the EHLS. Participants who completed the Dichotic Digits Test (DDT) during the fourth examination period of the EHLS (2008–2010) or the second examination period of the BOSS (2010–2013) were included ( $n = 3,655$ , mean age = 61.1 years).

**Data Collection and Analysis:** The DDT-free recall test was conducted using 25 sets of triple-digit pairs at a 70 dB HL presentation level. The total number of correctly repeated digits from the right and left ears was converted to a percentage correct and used as an outcome. The percentage correct in the left ear was subtracted from the percentage correct in the right ear and used as an outcome. Vascular health–related measures obtained during the examination included blood pressure, mean carotid intima-media thickness, femoral pulse wave velocity (PWV), hemoglobin A1C, and non–high-density lipoprotein (HDL) cholesterol, and, in the EHLS participants, C-reactive protein and interleukin-6. Information on vascular health–related history and behaviors was self-reported. General linear modeling produced estimates of the age- and sex-adjusted least squares means for each vascular factor, and multiple linear regression was used for multivariable modeling of each outcome.

**Results:** After multivariable adjustment, participants with diabetes had a significantly lower (worse) mean DDT-free recall total score ( $-2.08$  percentage points,  $p < 0.001$ ) than those without diabetes.

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\*Department of Ophthalmology and Visual Sciences, University of Wisconsin, Madison, WI; †Department of Population Health Sciences, University of Wisconsin, Madison, WI; ‡Department of Communication Sciences and Disorders, University of Wisconsin, Madison, WI; §Division of Epidemiology and Community Health, University of Minnesota, Minneapolis, MN

Corresponding author: Mary E. Fischer, Department of Ophthalmology and Visual Sciences, School of Medicine and Public Health, University of Wisconsin-Madison, Madison, WI 53726-2336; Email: fischer@episense.wisc.edu

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Participants who exercised at least once per week had a significantly higher (better) mean DDT-free recall total score (+1.07 percentage points,  $p < 0.01$ ) than those who did not exercise at least once per week. Alcohol consumption was associated with a higher DDT-free recall total score (+0.15 percentage points per +25 g ethanol,  $p < 0.01$ ). In multivariable modeling of the right–left ear difference in DDT-free recall scores, participants with a history of cardiovascular disease (CVD) or higher PWV demonstrated significantly larger differences (CVD: +3.11 percentage points,  $p = 0.02$ ; PWV: +0.36 percentage points per 1 m/sec,  $p < 0.01$ ). Higher levels of non-HDL cholesterol were associated with smaller right–left ear differences (−0.22 percentage points per 10 mg/dL,  $p = 0.01$ ). Adjustment for handedness did not affect the results.

**Conclusions:** Vascular health–related factors may play a role in central auditory function.

**Key Words:** central auditory function, dichotic listening tests, epidemiology, vascular health–related factors

**Abbreviations:** BMI = body mass index; BOSS = Beaver Dam Offspring Study; CRP = C-reactive protein; CVD = cardiovascular disease; DDT = Dichotic Digits Test; EHLS = Epidemiology of Hearing Loss Study; GHb = glycosylated hemoglobin; HDL = high-density lipoprotein; IL-6 = interleukin-6; IMT = intima-media thickness; PTA = pure-tone average; PWV = pulse wave velocity; REA = right ear advantage

## INTRODUCTION

Central auditory processing dysfunction has been found to be related to cognitive dysfunction, including decline, impairment, and dementia (Hällgren et al, 2001; Gates et al, 2002; 2008; 2010; 2011; Idrizbegovic et al, 2013; Fischer et al, 2017). The Dichotic Digits Test (DDT) is one of many measures used to evaluate central auditory processing (Musiek et al, 1991; Gates et al, 2008; 2010; 2011). In the DDT, single-syllable numbers, typically in double-digit or triple-digit pairs, are presented in both ears concurrently, and in the free recall version of the test, individuals are asked to repeat all numbers. One reason that the DDT, as well as other dichotic speech recognition tests, is particularly cognitively challenging may be because the competing signals result in the suppression of the ipsilateral processing pathways and consequently in more reliance on the contralateral pathways (Hugdahl, 1995).

Older age is strongly related to poor performance on central auditory processing tests (Jergler et al, 1994; Wilson and Jaffe, 1996; Strouse et al, 2000; Hällgren et al, 2001; Gates et al, 2002; 2011; Roup et al, 2006; Fischer et al, 2017) and to a greater right ear advantage (REA) in recall of the presented material (Wilson and Jaffe, 1996; Strouse and Wilson, 1999a; Roup et al, 2006; Hommet et al, 2010; Fischer et al, 2017). A recent population study reported that females and those with a college degree performed significantly better on the DDT-free recall (Fischer et al, 2017). The Blue Mountains Hearing Study also found better performance by females on dichotic listening tests (Golding et al, 2006), but few additional factors have been studied or reported to be related to dichotic testing on a population level.

With respect to the relationship between vascular health–related factors and central auditory processing, a cross-sectional study in the Framingham cohort reported that a history of heart attack or stroke in women and current smoking in men were related to performance

on the Synthetic Sentence Identification test, a test with competing message (Gates et al, 1993), and in a recent case–control study of patients with stroke, cases had significantly higher rates of central auditory processing deficits than controls (Koochi et al, 2017). It has also been reported that individuals with type 2 diabetes had higher speech thresholds in the Hearing in Noise Test (Frisina et al, 2006). Associations between vascular health–related factors and pure-tone threshold hearing loss have been found as well (Gates et al, 1993; Cruickshanks, Klein, et al, 1998; Bainbridge et al, 2008; Kiely et al, 2012; Cruickshanks et al, 2015; Fischer et al, 2015). Factors found to be associated with the risk of hearing impairment in previous prospective studies include current smoking, waist circumference, and glycosylated hemoglobin (GHb) (Cruickshanks et al, 2015), and subclinical atherosclerosis, as measured by carotid intima-media thickness (IMT) and plaque, and body mass index (BMI) (Fischer et al, 2015). Baseline hypertension has been reported to be related to hearing decline over an 11-year follow-up (Kiely et al, 2012), and findings from cross-sectional investigations have suggested associations between hearing loss and smoking (Cruickshanks, Klein, et al, 1998), coronary heart disease (Gates et al, 1993), and diabetes (Bainbridge et al, 2008). Physical exercise has been found to be inversely related to self-reported hearing problems (Curhan et al, 2013).

The aim of this study was to evaluate, on a population level, the relationship of vascular health–related factors with central auditory function. The total score on the DDT-free recall test was used as the measure of central auditory processing, and vascular health–related history, measurements, and behavioral factors were considered as potential-related factors. The relationship between these same factors and the right–left ear difference on the DDT-free recall test was also evaluated. The results may be useful in planning future prospective investigations of the predictors of central auditory decline or dysfunction.

## METHODS

### Study Population

Participants were part of the Epidemiology of Hearing Loss Study (EHLS) or the Beaver Dam Offspring Study (BOSS)—prospective longitudinal studies of aging and sensory disorders. Participants from the baseline Beaver Dam Eye Study (1987–1988) were eligible to participate in the EHLS, and there were 3,753 participants with an age range of 48–92 years in the EHLS baseline examination (1993–1995). Follow-up examinations occurred at 5-year intervals, with >80% response rates. The data in the present study are from the fourth examination period of the EHLS (2008–2010). Audiometric testing was administered to 1,549 participants, of which 1,391 completed free recall and right ear-directed dichotic digits testing (Fischer et al, 2017). Reasons for not completing dichotic digits testing include hearing loss severity or asymmetry ( $n = 103$ ), not successfully completing the dichotic digits training exercise ( $n = 13$ ), requesting to stop ( $n = 14$ ), or other/unknown reasons ( $n = 28$ ). Details of the EHLS are found in previous reports (Klein et al, 1991; Cruickshanks, Wiley, et al, 1998; Cruickshanks et al, 2003; 2010).

The adult offspring of the EHLS participants were eligible for the BOSS. At the time of the BOSS baseline examination (2005–2008), there were 3,296 participants with an age range of 21–84 years. During the 5-year follow-up examination (2010–2013), audiometric data were obtained from 2,346 participants and dichotic digits testing data from 2,264 participants. The reasons for not completing dichotic digits testing were ineligibility due to hearing loss severity or asymmetry ( $n = 28$ ), not successfully completing the training ( $n = 11$ ), requesting to stop ( $n = 26$ ), or other/unknown reasons ( $n = 17$ ). Further details of the BOSS are found in previous reports (Zhan et al, 2010; Nash et al, 2011; Fischer et al, 2013; 2015).

There was a total of 3,655 subjects (1,600 men and 2,055 women) included in the study, with an average age of 61.1 years. Close to 4% of the study population were aged younger than 40 years, 42% were 40–59 years, 45% were 60–79 years, and 9% were 80 years of age or older.

Approval for this research was obtained from the Health Sciences Institutional Review Board of the University of Wisconsin, and informed consent was obtained from all participants before each examination.

### Measurements

Participants underwent a series of standardized examinations and interviews, which were conducted by examiners who were trained and certified in all study protocols. Similar methods were used in the EHLS and BOSS.

### Audiometric Testing

Audiometric testing was performed, and hearing-related medical history questionnaires were administered. Testing was performed in accordance with American Speech-Language-Hearing Association guidelines in compliance with the American National Standards Institute standards (ASHA, 1978; ANSI, 1999; 2010). Otoscopy and tympanometry were performed before pure-tone audiometry. Testing was performed in sound-treated booths using clinical audiometers (calibrated every 6 months), TDH-50P earphones and ER3-A inserts in cases of probable ear canal collapse. There were 49 participants tested using insert earphones in other locations. Pure-tone air-conduction thresholds were obtained in both ears at 0.5, 1, 2, 3, 4, 6, and 8 kHz, and bone-conduction thresholds were obtained at 0.5, 2, and 4 kHz. Masking was used as necessary (Cruickshanks, Wiley, et al, 1998; Cruickshanks et al, 2003). A four-frequency pure-tone average (PTA) at 0.5, 1, 2, and 4 kHz was calculated for each ear and used to categorize hearing loss severity of either ear (worse ear) as follows: no loss =  $PTA \leq 25$  dB HL ( $n = 2,412$ , mean PTA = 12.8 dB HL); mild loss =  $25 < PTA \leq 40$  dB HL ( $n = 799$ , mean PTA = 32.1 dB HL); and moderate or marked loss =  $PTA > 40$  dB HL ( $n = 444$ , mean PTA = 49.3 dB HL). There were 3,067 participants with symmetrical hearing loss severity (both ears were in the same severity group), 221 participants in whom the right ear loss was more severe than the left ear, and 367 participants in whom the left ear loss was more severe than the right ear.

### DDT

To complete the DDT, participants had to accurately complete a training/practice task, in which three examples of single-digit, double-digit, and triple-digit pairs were presented. If the participant was unable to repeat any of the numbers in the single-digit or double-digit pairs or did not attempt to repeat any of the numbers in the triple-digit pairs, the participant was not tested on the DDT. The free recall and right ear-directed recall conditions each consisted of 25 sets of triple-digit pairs (three digits presented to each ear simultaneously) using single-syllable numbers 1 through 10, excluding 7, presented at 70 dB HL. The CD for the test was provided by Dr. Richard Wilson. In the free recall task, which was administered first, the participant was asked to repeat as many of the six digits as possible. The numbers of correctly repeated digits from the right and left ears was added together, and the sum was used as the score for the DDT-free recall. The possible range of the score was 0–150 (75 per ear). The number correct was converted into percentage correct for analysis purposes. The right-left ear difference was calculated by

subtracting the left ear percentage correct from the right ear percentage correct.

### Vascular Health–Related Factors

A history of cardiovascular disease (CVD) was defined as a self-report of a physician-diagnosed stroke, angina, or myocardial infarction. Hypertension was defined as having received a diagnosis of hypertension with current medication use or having a measured systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg. Diabetes was defined as a self-report of a physician diagnosis or a suspected diagnosis with current treatment, or as having a hemoglobin A1C  $\geq 6.5\%$ . The assay used to determine hemoglobin A1C used the Tosoh HPLC G7 Glycohemoglobin Analyzer (Tosoh Medics, Inc., San Francisco, CA) with nonfasting venous blood specimens. Cholesterol and high-density lipoprotein (HDL) cholesterol assays were performed using the Roche Modular P Chemistry Analyzer (Roche Diagnostics Corporation, Indianapolis, IN), and non-HDL cholesterol was determined by subtracting the HDL value from the total cholesterol value. BMI was calculated from measures of height and weight ( $\text{kg}/\text{m}^2$ ), and obesity was defined as  $\geq 30$   $\text{kg}/\text{m}^2$ .

The mean carotid IMT and the plaque score were determined through high-resolution B-mode carotid artery ultrasound (MyLab25; Esaote North America Inc., Indianapolis, IN). The IMT was measured in 1.0 cm segments of the near and far walls of the common artery, internal artery, and the carotid bifurcation. Ultrasound imaging and grading used a modified Atherosclerosis Risk in Communities protocol (Bond et al, 1991; Riley et al, 1991), and the mean of the 12 walls was calculated for the IMT measure. The mean IMT was categorized according to tertiles of the distribution as (1)  $\leq 0.6224$  mm, (2)  $> 0.6224$  mm and  $\leq 0.7783$  mm, and (3)  $> 0.7783$  mm. Plaque was considered to be present if acoustic shadowing was seen in association with at least one of the following, or if acoustic shadowing was not seen with at least two of the following: change in wall shape (protrusion into lumen), change in wall texture, or IMT  $> 1.5$  mm. The plaque score was defined as the number of sites (0–6) with plaque present (Zhong et al, 2012; Schubert et al, 2015). Femoral pulse wave velocity (PWV) was measured using the Complior SP System (Artech Medical/Alam Medical, Vincennes, France). The PWV from the right common carotid artery to the right femoral artery was measured at a time when the signal was clean, had a fast rising systole, sufficient systolic amplitude, a relatively flat diastole for at least ten cycles, and, when possible, a PWV tolerance  $< 5\%$  (Zhong et al, 2014; Schubert et al, 2015).

In EHLS participants, the C-reactive protein (CRP) level was determined (Advanced Research and Diagnostic Laboratory, University of Minnesota, Minneapolis,

MN) using a latex particle–enhanced immunoturbidimetric assay from Roche Diagnostics on the Roche Modular P Chemistry Analyzer (Roche Diagnostics Corporation) and was categorized into the following groups:  $< 1.0$ ,  $1.0$ – $3.0$ , and  $> 3.0$  mg/L. Serum interleukin-6 (IL-6) was measured using the quantitative sandwich enzyme technique of the enzyme-linked immunosorbent assay (QuantiKine High Sensitivity kit; R&D Systems, Minneapolis, MN) and was categorized into the following tertiles based on the distribution:  $\leq 1.192$ ,  $> 1.192$  and  $\leq 2.252$ , and  $> 2.252$  pg/mL. A summary measure of the number of inflammatory markers in the highest category was created (range: 0–2). Additional details of the CRP and IL-6 assays have been reported (Nash et al, 2013; Wichmann et al, 2014).

Self-reported smoking status was classified as non-smoker ( $< 100$  cigarettes in lifetime), ex-smoker, or current smoker. Alcohol consumption was measured by a quantity/frequency questionnaire and converted to grams of ethanol per week. Ever having consumed heavy alcohol was defined as ever drinking 4+ drinks per day. Exercise was defined as being sufficient to work up a sweat at least once a week.

### Covariates

Demographic factors used in the analysis were age, sex, and education. Education was categorized as less than a high school graduate ( $< 12$  years), a high school graduate (12 years), some college (13–15 years), and college graduate or beyond (16+ years).

Handedness was determined by asking “Are you right or left handed?” with possible answers of “Left,” “Right,” “Use both equally,” or “Unknown.” Cognition was measured with the Mini-Mental State Examination test (Folstein et al, 1975). The test was administered to participants aged 50 years and older; participants younger than 50 years were assumed to have no cognitive impairment. If the Mini-Mental State Examination score was  $< 24$  (of a maximum of 30), or if there was a self- or proxy-reported history of dementia or Alzheimer’s disease, the subject was considered to have cognitive impairment.

### Statistical Analyses

All analyses were completed using SAS version 9.4 software (SAS Institute, Inc., Cary, NC).

General linear modeling was used to assess the age- and sex-adjusted associations of the categorically measured vascular health–related factors with the DDT-free recall total score and to estimate age- and sex-adjusted least squares means. Categorical covariates were modeled using indicator variables. To allow for estimates proportional to the observed margins, the ObsMargins option was used. Multiple linear regression was performed to

evaluate the age- and sex-adjusted associations of the continuously measured factors with the DDT-free recall total score.

Multiple linear regression was used for multivariable modeling, with the significant factors from the age- and sex-adjusted models included in the full multivariable model. The covariates previously identified as being significantly related to the DDT-free recall total score, namely age, sex, education, hearing loss severity, and cognitive impairment (Fischer et al, 2017), were also included in the multivariable model. Indicator variables were used in the models for the education groups, with the college graduate category as the reference group. Indicator variables were also used for the hearing loss severity groups, with the no loss group as the reference. Cognitive impairment was a dichotomous variable. A final, reduced model was developed through the elimination of nonsignificant independent variables.

The modeling approach used for the DDT-free recall total score was followed for the right–left ear difference in percentage correct as the outcome.

## RESULTS

The range of the free recall scores was 21.3% to 100%, with a mean of 76.7%. Additional descriptive information on the study population and the distribution of the DDT scores has been reported (Fischer et al, 2017). In age- and sex-adjusted models, participants with a reported history of CVD had a mean total free recall score that was 2.0 percentage points lower ( $p < 0.01$ ) than participants without CVD, and those with diabetes had an average total free recall score that was 3.0 percentage points lower ( $p < 0.0001$ ) than those without diabetes (Table 1). Hypertension was not strongly related to the total score. Obesity was significantly ( $p < 0.001$ ) associated with the total DDT-free recall score whereby participants who were obese had a mean score of 1.3 percentage points lower than the non-obese. Physical exercise was found to be related to a higher adjusted mean score (77.6% in those who exercised at least once/week versus 75.5% in those who did not;  $p < 0.0001$ ), but smoking was not related. A history of heavy alcohol use was negatively associated (–1.9 percentage points) with DDT-free recall performance, whereas current alcohol consumption was positively associated with performance (+0.19 percentage points in total score per 25 g ethanol increase). The mean IMT, plaque count, non-HDL cholesterol, and femoral PWV were not significantly associated with performance.

In a multivariable model, diabetes was associated with a lower DDT-free recall score (–2.08 percentage points,  $p < 0.001$ ) (Table 2). Alcohol consumption and exercise were associated with higher DDT-free recall scores (+0.15 percentage points per +25 g ethanol and +1.07 percentage points if exercise at least once/week,  $p < 0.01$  for each). CVD

history and obesity were no longer significantly related to the DDT-free recall score in the multivariable models. However, if diabetes was removed from the multivariable model, CVD history was significant (–1.64 percentage points,  $p = 0.01$ ) and obesity was close to significant (–0.70 percentage points,  $p = 0.06$ ). No significant relationship was observed in the EHLS participants between the DDT-free recall total score and high levels of CRP and IL-6 (age- and sex-adjusted mean score by the number of high markers: 0 = 71.6%, 1 = 72.3%, and 2 = 71.4%;  $p = 0.60$ ). If a history of heavy alcohol use was included in the multivariable model in place of current alcohol consumption, it was not significantly related to the total DDT-free recall score ( $p = 0.15$ ).

The overall mean right–left ear difference, or REA, in DDT-free recall scores was 14.7 percentage points (Table 3). Information on the distribution of the right–left ear difference in DDT scores has been previously reported (Fischer et al, 2017). In age- and sex-adjusted models, CVD, diabetes, and a history of heavy alcohol use some time in the past were significantly associated with a greater adjusted mean right–left ear difference (CVD: +2.5 percentage points,  $p = 0.03$ ; diabetes: +3.3 percentage points,  $p < 0.001$ ; and heavy alcohol use: +1.9 percentage points,  $p = 0.03$ ). Non-HDL cholesterol (–0.21 percentage points per +10 mg/dL,  $p = 0.02$ ) and femoral PWV (+0.36 percentage points per 1 m/sec,  $p < 0.01$ ) were also significantly related to the right–left ear difference in DDT-free recall scores. Hypertension, obesity, smoking, exercise, mean IMT, plaque, and weekly alcohol consumption were not associated with the difference. In a multivariable model, effect estimates were similar to those in the age- and sex-adjusted models (CVD: +3.11 percentage points,  $p = 0.02$ ; non-HDL cholesterol: –0.22 percentage points per 10 mg/dL,  $p = 0.01$ ; and femoral PWV: +0.36 percentage points per 1 m/sec,  $p < 0.01$ ) (Table 4). However, diabetes and heavy alcohol use were no longer significant. Adjustment for handedness altered the effect estimates very little (CVD: +3.04 percentage points,  $p = 0.02$ ; non-HDL cholesterol: –0.22 percentage points per 10 mg/dL,  $p = 0.01$ ; and femoral PWV: +0.37 percentage points per 1 m/sec,  $p < 0.01$ ).

## DISCUSSION

Associations between vascular health–related factors and the DDT-free recall total score and right–left ear difference were observed in this cross-sectional study, suggesting that vascular health and central auditory function may be connected. Diabetes was associated with lower DDT-free recall total scores, whereas exercise and alcohol consumption were associated with higher total scores. Effects were modest in size and although statistically significant, they may not be clinically significant. However, in previous cross-sectional work in the same study cohort, a difference of –1% in the DDT total free recall score was observed for every +5 years of age (Fischer et al, 2017). Therefore, the

**Table 1. Free Recall DDT Score (%) Age- and Sex-Adjusted Means by Potential-Related Factors**

	N (%)	Free Recall (%)	
		Mean	p-Value
Overall	3,655 (100.0)	76.7	–
Categorically measured factors			
Cardiovascular disease history			<0.01
Yes	343 (9.4)	74.9	
No	3,294 (90.6)	76.9	
Hypertension			0.24
Yes	1,888 (51.9)	76.5	
No	1,752 (48.1)	77.0	
Diabetes			<0.0001
Yes	512 (14.0)	74.1	
No	3,135 (86.0)	77.1	
Obesity (BMI ≥ 30.0 kg/m <sup>2</sup> )			<0.001
Yes	1,785 (49.9)	76.1	
No	1,791 (50.1)	77.4	
Smoking status			0.40
Never	1,882 (51.6)	76.7	
Former	1,351 (37.0)	76.8	
Current	416 (11.4)	76.0	
Ever heavy alcohol			<0.001
Yes	731 (20.5)	75.1	
No	2,836 (79.5)	77.0	
Exercise at least 1×/week			<0.0001
Yes	2,025 (55.5)	77.6	
No	1,622 (44.5)	75.5	
Mean IMT (tertiles)			0.24
1	1,201 (33.3)	76.3	
2	1,204 (33.4)	77.2	
3	1,201 (33.3)	76.9	
Plaque count			0.26
0	1,536 (43.5)	77.1	
1–3	1,618 (45.8)	76.9	
4–6	377 (10.7)	75.9	
	Mean (Standard Deviation)	Free Recall (%)	
		β	p-Value
Continuously measured factors			
Alcohol consumption/week (β: per 25 g)	50.8 (95.1)	0.19	<0.001
Non-HDL cholesterol (β: per 10 mg/dL)	143.5 (39.1)	0.08	0.11
PWV—femoral (β: per 1 m/sec)	9.8 (2.7)	–0.03	0.68

diabetes effect found in the present study could be thought of as roughly equivalent to +10 years of age, whereas the exercise effect could be thought of as

roughly equivalent to –5 years of age. CVD history and a greater femoral PWV were significantly related to a greater right–left ear difference in free recall scores.

**Table 2. Free Recall DDT Score (%) Multivariable-Adjusted Linear Regression Models**

	Free Recall DDT Score (%)					
	Full (n = 3,538)			Reduced (n = 3,627)		
	B (%)	Standard Error	p-Value	β	Standard Error	p-Value
Cardiovascular disease history	–1.06	0.66	0.11	–	–	–
Diabetes	–1.66	0.57	<0.01	–2.08	0.54	<0.001
Obesity	–0.52	0.38	0.17	–	–	–
Exercise at least 1×/week	1.05	0.38	<0.01	1.07	0.38	<0.01
Alcohol consumption/week (per 25 g)	0.15	0.05	<0.01	0.15	0.05	<0.01

Also includes adjustment for age, sex, education, hearing loss severity, and cognitive impairment.

**Table 3. Right Ear Minus Left Ear Free Recall DDT Scores (%) Age- and Sex-Adjusted Mean Difference by Potential-Related Factors**

	Free Recall Right–Left Ear Difference (%)	
	Mean	<i>p</i> -Value
Overall	14.7	–
Categorically measured factors		
Cardiovascular disease history		0.03
Yes	16.9	
No	14.4	
Hypertension		0.39
Yes	14.9	
No	14.3	
Diabetes		<0.001
Yes	17.5	
No	14.2	
Obesity (BMI $\geq$ 30.0 kg/m <sup>2</sup> )		0.20
Yes	15.1	
No	14.2	
Smoking status		0.55
Never	14.4	
Former	15.1	
Current	14.3	
Ever heavy alcohol		0.03
Yes	16.2	
No	14.3	
Exercise at least 1 $\times$ /week		0.61
Yes	14.5	
No	14.9	
Mean IMT (tertiles)		0.56
1	15.3	
2	14.5	
3	14.2	
Plaque count		0.96
0	14.7	
1–3	14.7	
4–6	14.3	
Free Recall Right–Left Ear Difference (%)		
	$\beta$	<i>p</i> -Value
Continuously measured factors		
Alcohol consumption/week ( $\beta$ : per 25 g)	–0.04	0.65
Non-HDL cholesterol ( $\beta$ : per 10 mg/dL)	–0.21	0.02
PWV—femoral ( $\beta$ : per 1 m/sec)	0.36	<0.01

These relationships were independent of any confounding effects of age, sex, education, hearing loss severity, and cognitive impairment.

It has been suggested that auditory perception and speech communication are dependent on the interaction between hearing function, central auditory processing, and cognitive function (Humes et al, 2012). Therefore, performance on tests of speech in noise or dichotic listening is likely dependent on all three of these functions. Although vascular health–related factors have been found to be associated with auditory thresholds and cognitive function in previous studies, the current study adds to these findings by focusing on a central auditory processing

test. Adjustments for the effects of hearing loss severity and cognitive impairment were made to evaluate the independent relationships of the vascular factors with central auditory processing.

Previous studies reporting a relationship of vascular health–related factors with hearing function, change, and impairment, using audiometric threshold measures, have included prospective (Kiely et al, 2012; Linssen et al, 2014; Nash et al, 2014; Cruickshanks et al, 2015; Fischer et al, 2015) and cross-sectional investigations (Gates et al, 1993; Cruickshanks, Klein, et al, 1998; Bainbridge et al, 2008; Helzner et al, 2011). Among the findings from these studies was a report that high

**Table 4. Right Ear Minus Left Ear Free Recall DDT Scores (%) Multivariable-Adjusted Linear Regression Models**

	Free Recall Right–Left Ear Difference (%)					
	Full (n = 3,261)			Reduced (n = 3,339)		
	B (%)	Standard Error	p-Value	$\beta$	Standard Error	p-Value
Cardiovascular disease history	3.04	1.31	0.02	3.11	1.28	0.02
Diabetes	1.22	1.07	0.25	–	–	–
Ever heavy alcohol	0.78	0.90	0.39	–	–	–
Non-HDL cholesterol (per 10 mg/dL)	–0.23	0.09	0.01	–0.22	0.09	0.01
PWV—femoral (per 1 m/sec)	0.35	0.14	0.01	0.36	0.14	<0.01

Also includes adjustment for age, sex, education, hearing loss severity, and cognitive impairment.

GHb (>12%) was related to a twofold increased risk of hearing impairment over a 15-year follow-up (Cruickshanks et al, 2015). However, there was not a significant association of hearing impairment risk with diabetes (self-reported doctor diagnosis or a GHb > 8%) or with other levels of GHb; the increased risk was confined to those with high GHb. A cross-sectional study using self-reported doctor-diagnosed diabetes found that individuals with diabetes had an 80% increased likelihood of having a hearing impairment in the low–mid frequencies and were over twice as likely to have a high-frequency impairment (Bainbridge et al, 2008). Adjustment for cardiovascular, inflammatory, and neuropathic factors attenuated these relationships, although they remained significant (Bainbridge et al, 2010). A third study, a case–control study of type 2 diabetes, found that controls had significantly shorter suprathreshold gap detection thresholds and lower speech thresholds than cases in the Hearing in Noise Test with background noise (Frisina et al, 2006). It is noteworthy that performance on these two tests is dependent not only on auditory thresholds but also on central auditory processing. The current study supports these findings, as it also found higher DDT scores among participants without diabetes.

The present study also found that exercise and alcohol consumption were associated with higher DDT-free recall scores. Research has been conducted investigating possible protective effects of physical activity (Paffenbarger et al, 1978; Folsom et al, 1997; Jakovljevic, 2017) and moderate alcohol consumption (Friedman and Kimball, 1986; Fuchs et al, 1995; Lucas et al, 2005) on vascular health–related conditions and events for many years, but physical activity and alcohol consumption have generally not been widely studied in relation to hearing loss. In previous work related to physical activity, it has been reported that participants who exercised at least once/week had a slightly (–1 dB), but significantly, lower PTA<sub>0.5,1,2,4 kHz</sub> at a 5-year follow-up examination (Fischer et al, 2015). In addition, in a study of self-reported hearing problems, higher physical activity has been found to be protective (Curhan et al, 2013). In two prospective investigations, alcohol consumption was not found to be significantly related to

hearing impairment risk (Cruickshanks et al, 2015; Fischer et al, 2015).

The concept of an REA in dichotic listening tests (Kimura, 1961), in which performance is better for material presented to the right ear than the left ear, has been previously studied, but little work has been done investigating factors related to the REA other than age and handedness. The hypothesized explanation for the REA is that through the crossed afferent auditory pathway, the right ear is linked to the left hemisphere of the brain that specializes in verbal processing. Because the left ear signals are routed to the right hemisphere, inter-hemispheric transfer through the corpus callosum must take place for recognition of verbal stimuli from the left ear. With age and possible age-related neurodegeneration, this transfer may become less effective in a dichotic listening situation (Jerger et al, 1995; Greenwald and Jerger, 2001). A greater REA has been found in older ages (Wilson and Jaffe, 1996; Strouse and Wilson, 1999a,b; Roup et al, 2006; Fischer et al, 2017) perhaps as a result of a more pronounced age effect on left ear performance than right ear performance.

Recently, a greater REA was found to be related to a lower education level and the presence of cognitive impairment (Fischer et al, 2017) which is compatible with early findings, suggesting that as the difficulty of the task increases, the REA increases (Strouse and Wilson, 1999a,b). In the present study, a greater REA was associated with CVD history and higher femoral PWV, a measure of arterial stiffness, findings which are in line with previous work evaluating the relationship between these measures and cognitive functioning. Greater carotid artery IMT, a measure of generalized atherosclerosis, was found to be associated with an increased risk of cognitive impairment over 10 years (Zhong et al, 2012), and a higher Framingham CVD risk score was reported to be related cross-sectionally to lower cognitive test performance in both sexes and prospectively to cognitive decline in men (Kaffashian et al, 2011). A negative association between femoral PWV and cognitive function has been reported whereby a PWV > 12 m/sec was associated with lower cognitive test scores (Zhong et al, 2014). Other studies, including prospective investigations, have



reported a similar negative association with at least some cognitive tests (Waldstein et al, 2008; Mitchell et al, 2011; Watson et al, 2011), although not all have found significant associations (Poels et al, 2007).

The observed relationships in the current study and previous work may be a result of the potential impact of microvascular changes such as small vessel damage and of various pathophysiologic changes accompanying vascular disease including reduced blood flow. For example, internal auditory artery narrowing and demyelination of the eighth cranial nerve along with thickening of the capillaries in the stria vascularis and spiral ganglion atrophy have been found in autopsied diabetic subjects (Bainbridge et al, 2010). The state of hyperglycemia may affect the central nervous system as well as the inner ear (Frisina et al, 2006), and the oxidative damage, greater apoptosis, and disruption of metabolic processes that accompany prolonged hyperglycemia may result in neurodegenerative damage. By contrast, regular physical activity may be beneficial for auditory function through mechanisms such as improved endothelial function and reduced oxidative stress and may provide neuroprotective effects on central auditory processing (Curhan et al, 2013). For example, regular physical activity has been shown to be associated with lower aortic PWV (less stiffening) (Vaitkevicius et al, 1993; Tanaka et al, 1998) perhaps as a result of reduced oxidative stress (Seals et al, 2009). The physiologic consequences of arterial stiffness include reduced blood flow to the brain and small vessel damage (O'Rourke and Safar, 2005).

The strengths of this study include the large size ( $n = 3,655$ ) of the study population and the wide age range of the participants (nearly 80-year age span). Information on numerous vascular health conditions and measures was available for evaluation. Similar protocols were followed by trained and certified examiners in the EHLS and the BOSS, so data from the two cohorts could be combined. The test-retest reliability of the DDT has been shown to be good (Strouse and Wilson, 1999a), although the methodology used in the reliability assessment randomly presented one-, two-, and three-digit pair modalities, which is a departure from the methodology used in the present study, and the participants were on average younger (mean age = 49.4 years), with a larger percentage of men (72%) than women in the present study. Although much of the previous work with dichotic listening tests have evaluated ear-specific function, the total of the right and left ear DDT scores was used as one of the outcomes in the current study. The objective of this study was to investigate the relationship between vascular health-related factors and DDT performance on a population level. The total score was a comprehensive measure of overall performance. With respect to limitations, the study was cross-sectional; therefore, temporal relationships cannot be inferred. The significant factors found to be related to the DDT-free

recall total score and the right-left ear difference were not the same in the present study, but this lack of consistency may be a reflection of the different aspects of central auditory processing that they each measure. The DDT-free recall total score provides a summary measure of DDT performance. By contrast, as a difference measure, the right-left ear difference does not include information on how well participants performed. For example, one participant could have scored 95% in the right ear and 90% in the left ear and another participant could have scored 75% in the right ear and 70% in the left ear; both participants had a right-left ear difference of 5%, but they performed very differently on the test. Therefore, the DDT-free recall total score was evaluated to determine factors associated with overall central auditory processing function. The right-left ear difference was evaluated to determine factors associated with the right ear advantage without regard to the performance level. The difference in findings between the total score and the right-left ear difference with respect to CVD history may also be related to the possibility that CVD and diabetes share a common effect on the DDT-free recall total score; CVD history was significant when diabetes was not included in the multi-variable modeling. Finally, although the DDT right ear-directed recall was administered, there was not sufficient variability in performance to allow for the investigation of vascular health-related factors.

The present study found a relationship of a number of vascular health-related factors with performance on the DDT-free recall. Relationships were found when evaluating the DDT-free recall total score as well as the right-left ear difference in the DDT-free recall scores. These results suggest that vascular health-related factors, including modifiable behaviors, may play a role in central auditory function, and these factors should be considered as possible predictors of central auditory decline or dysfunction in future prospective investigations.

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